

DENGUE VIRUS INFECTION IN EARLY GESTATION WITH DELIVERY OF AN UNAFFECTED FETUS AND NO VERTICAL TRANSMISSION

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Dengue fever is an infectious, tropical viral disease. There have been a number of epidemics in Taiwan during the last century [1]. In addition, dengue hemorrhagic fever (DHF) and even dengue shock fever have been reported in recent decades. Dengue infection may cause disease in neonates born to infected mothers, but the teratogenic and abortion effects of dengue infection on pregnant women and their fetuses, especially during early gestation, are unclear. Prenatal genetic counseling is, therefore, crucial. Here, we present a pregnant woman of 11⁺ weeks' gestation who suffered from DHF, but finally gave birth to an unaffected full-term baby.

A 30-year-old, gravida 2, para 1, woman at 11⁺ weeks' gestation was sent to our emergency department with a 3-day history of intermittent high fever (> 39°C) and headache. Her previous obstetric history and prenatal care were uneventful. Her body temperature was 38.4°C, and the results of urine analysis were within normal limits. Her white blood cell count was 7,100/μL, and her platelet count was 245,000/μL (Figure). The cause of her fever remained undetermined after the initial workup.

After triage, the patient was admitted to the infection ward. She was also closely monitored for serial full blood counts and urea levels, and by liver function tests and fetal echographic screening. Three days later, she developed nausea, petechiae, severe thrombocytopenia, and leucopenia (Figure). Her body temperature rose to a maximum of 39.7°C, and her platelet count dropped

to 25,000/μL on the sixth day after admission (Figure). Acute dengue virus infection was highly suspected based on the patient's reported recent mosquito bite history, and this was subsequently confirmed by serologic tests. She was provided with supportive care, and the fever gradually subsided. Her blood platelet count had increased to normal by the ninth day. Regular prenatal care was arranged after discharge at our obstetrics outpatient department. An uncomplicated pregnancy led to the delivery of a normal healthy male infant at 39 weeks' gestation. Delivery was by cesarean section owing to a breech presentation. Serologic testing for immunoglobulins, IgG and IgM, against dengue virus was negative in the neonate, although IgG was still detected in the mother after delivery.

Dengue fever is a major public health concern in Taiwan and in other countries in Southeast Asia.

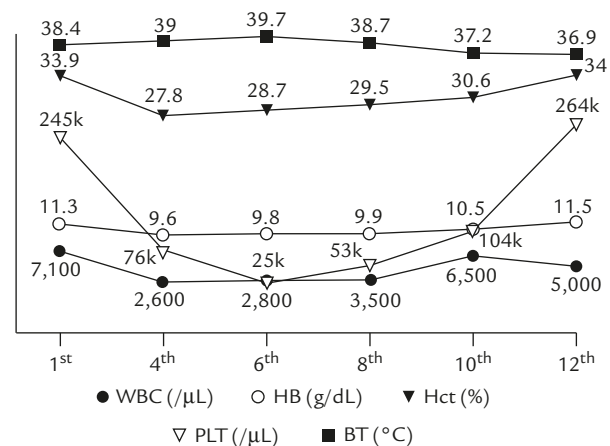


Figure. Graph showing changes in white blood cell (WBC) counts, hemoglobin (HB), hematocrit (Hct), platelet (PLT) counts, and body temperature (BT). The horizontal axis represents the date post-admission.



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Urbanization, increased population densities, more frequent air travel and limited resources for prevention mean that epidemic countries pay considerable attention to infectious disease control. The epidemiology of dengue infection has continued to change over the decades. In many endemic countries, the average age of first dengue infection is increasing, and dengue infection during pregnancy is likely to be encountered more frequently. For example, most women in Thailand are seropositive by the time they reach childbearing age. In a cross-sectional seroprevalence study in Bangkok between April and May 2000, the overall rate of seropositivity was 94.7%, and this increased with advancing maternal age [2]. Thus, young women have a greater risk of infection. Dengue infection is, therefore, an important threat to pregnant women in endemic areas, and can have major impacts on both the mother and the infant. However, there is limited evidence to show the effects of dengue infection on pregnancy outcome, the level of vertical transmission, and the teratogenic effects of maternal infection during early gestation.

Pregnancy does not generally alter the disease presentation or clinical course. Most patients are diagnosed clinically, and the diagnosis is subsequently confirmed by laboratory tests. Sirinavin et al [3] reported that 13/14 cases (93%) had typical presentations of abrupt fever accompanied by headache, retro-orbital pain, muscle aches, and thrombocytopenia. In some cases, these symptoms may be accompanied by hemoconcentration, pleural effusion, and shock [4]. Similarly, our case had a normal clinical presentation of acute dengue fever. It should be noted that although most dengue infections occur during the summer, our case occurred in early winter. This may be related to global warming and epidemiologic changes. Although the current case occurred during a non-epidemic season, dengue fever should be suspected in any patient with an atypical presentation and the appropriate laboratory studies should be initiated.

Dengue infection can occur during all three trimesters of pregnancy. Waduge et al [5] reported incidences of 3.8% (1/26), 7.7% (2/26), 77% (20/26), and 11.5% (3/26) in the first, second and third trimesters and during the immediate postpartum period in Sri Lanka, respectively. There was no association between disease severity and the timing of maternal infection, but the first attack of dengue fever (primary dengue) may predispose towards a much more severe illness following infection with other serotypes (secondary dengue) [6]. Most patients respond well to conservative management including bed rest and antipyretic agents. Serial platelet counts and platelet transfusions are mandatory strategies in patients with

DHF. Cesarean section may be considered, based on other obstetric indications.

The risk of maternal and neonatal complications should be addressed when dengue fever occurs in pregnant women. The main reported complications include premature delivery, severe and prolonged bleeding during cesarean deliveries, and a higher incidence of fetal death [5,7,8]. The mechanisms are unclear, but may be related to adverse effects of the dengue virus on the placenta or during its circulation. In the current case, we suggested that the mother undergo cordocentesis for the above reason, but the patient refused. However, Waduge et al [5] reported that no fetal malformations were found in any fetuses, although one patient who developed DHF in the first trimester had an abortion while suffering from acute symptoms of dengue. In another case series in India, two patients infected with dengue fever during the first trimester had uneventful pregnancy courses and delivered healthy babies [9]. The cases reported so far suggest that dengue infection during the first trimester may increase the risk of septic or threatened abortion, although the mechanism is not clear. However, the limited number of reports of mothers infected during this period are inadequate to allow conclusions on maternal and fetal outcomes to be drawn. In our case, no structural anomalies were identified by three-dimensional ultrasound performed during mid-term pregnancy. Although there have been a few reports of congenital fetal anomalies after dengue infection in early gestation, these may have been unrelated to the infection [10], and the fetus in our case was apparently unaffected. Detailed fetal echographic screening and genetic counseling regarding the risk of teratogenicity are, therefore, crucial.

Explaining the risk of vertical transmission to the patient during prenatal counseling is challenging. Previous studies found that most symptomatic congenital dengue infections occurred in neonates born to mothers infected very late in pregnancy. Insufficient protective antibodies may have developed in these cases to allow their transfer to the fetus. Management of such newborns includes diagnostic tests and close observation.

Furthermore, in one follow-up study of infants at 18 months old, antibodies to dengue virus had disappeared in 3% of babies by 2 months of age, in 19% by 4 months of age, in 72% by 6 months of age, in 99% by 9 months of age, and in 100% of babies by 12 months of age. Thus, antibodies to dengue virus had disappeared by the end of the first year of life [11]. If a vaccine were to become available, vaccination of infants in endemic areas at 1 year of age should be recommended. Although our knowledge of dengue fever during pregnancy is limited, conservative treatment seems to be sufficient.

However, fetal echographic screening should be mandatory at the follow-up prenatal examination.

In conclusion, dengue fever is a major public health concern in Taiwan and other countries in Southeast Asia. Dengue virus transmission occurs year-round but typically reaches a peak in summer. Dengue infection in late pregnancy is usually associated with an increased risk of maternal and neonatal complications. There is only limited evidence associating congenital anomalies with dengue infection during early gestation. Nevertheless, detailed fetal echographic screening and genetic counseling on the risks of teratogenicity are crucial. The present case provides further evidence to increase our knowledge of maternal-fetal medicine, and provides vital information for directing genetic counseling.

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